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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/789,536	02/26/2004	Arthur M. Krieg	C1039.70083US05	9640

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EXAMINER	
MINNIFIELD, NITA M	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
07/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/789,536	KRIEG ET AL.	
	Examiner	Art Unit	
	N. M. Minnifield	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37 and 39-56* is/are pending in the application.

4a) Of the above claim(s) *37,40-44,47-53,55 and 56* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45, 46 and 54* is/are rejected.

7)☒ Claim(s) *39* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/29/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicants' amendment filed February 25, 2008 is acknowledged and has been entered. Claims 1-36 and 38 have been canceled. Claims 37, 45, 46, 54 and 55 have been amended. Claims 37 and 39-56 are now pending in the present application. All rejections have been withdrawn in view of Applicants' amendment to the claims and/or comments, with the exception of those discussed below.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

3. The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

4. Claim 46 is are rejected under 35 U.S.C. 102(e) as being anticipated by Hutcherson et al (5723335) as evidenced by Gura et al (Science, 1995, 270:575-577).

The claim is directed to a method for stimulating a subjects response to a vaccine comprising administering an immunostimulatory oligonucleotide adjuvant as a vaccine adjuvant with the vaccine to the subject (human) to stimulate the subject's response to the vaccine, wherein the immunostimulatory oligonucleotide comprises a phosphate backbone modification and an unmethylated cytosine-guanine dinucleotide, wherein the oligonucleotide is at least eight nucleotides in length.

Hutcherson et al discloses a method of stimulating an immune response in a subject comprising administering to the subject an immunostimulatory oligonucleotide and a therapeutic (i.e. vaccine) can be administered to animals or humans (abstract; cols. 5-6). It has now been found, surprisingly, that oligonucleotide analogs having at least one phosphorothioate bond can induce stimulation of a local immune response. This immunostimulation does not appear to be related to any antisense effect (i.e. stimulation does not result from an antisense mechanism), which these oligonucleotide analogs may or may not possess. These oligonucleotide analogs are useful as immunopotentiators (i.e. adjuvant), either alone or in combination with other therapeutic modalities, such as drugs, particularly anti-infective and anticancer drugs, and surgical procedures to increase efficacy (cols. 4-5). It has also been found that oligonucleotide analogs having at least one phosphorothioate bond can be used to induce stimulation of a systemic or humoral immune response. Thus, these oligonucleotides are also useful as immunopotentiators of an antibody response, either alone or in combination

with other therapeutic modalities (i.e. vaccine). (col. 5) "The oligonucleotide analogs of this invention are used as immunopotentiators (i.e. adjuvant). For therapeutic or prophylactic treatment, oligonucleotide analogs are administered to animals, especially humans, in accordance with this invention. Oligonucleotides may be formulated in a pharmaceutical composition, which may include carriers, thickeners, diluents, buffers, preservatives, surface active agents and the like in addition to the oligonucleotide. Pharmaceutical compositions may also include one or more active ingredients such as antimicrobial agents, anti-inflammatory agents, anesthetics, and the like in addition to oligonucleotides. The pharmaceutical composition may be administered in a number of ways depending on whether local or systemic treatment is desired, and on the area to be treated. Administration may be done topically (including ophthalmically, vaginally, rectally, intranasally), intralesionally, orally, by inhalation, or parenterally, for example by intravenous drip or subcutaneous, intraperitoneal, intradermal or intramuscular injection. It is generally preferred to apply the oligonucleotide analogs in accordance with this invention topically, intralesionally or parenterally. Formulations for topical administration may include ointments, lotions, creams, gels, drops, suppositories, sprays, liquids and powders. Conventional pharmaceutical carriers, aqueous, powder or oily bases, thickeners and the like may be necessary or desirable. Compositions for oral administration include powders or granules, suspensions or solutions in water or non-aqueous media, capsules, sachets, or tablets. Thickeners, flavorings, diluents, emulsifiers, dispersing aids or binders may be desirable." (cols. 7-8) Hutcherson et al discloses that liposomes and cationic lipids can significantly enhance the uptake and fate of oligonucleotides and analogs as well as phosphate backbone modifications such as phosphorothioate (col. 8).

Hutcherson et al discloses the synthesis of oligonucleotides, which are unmethylated as evidence by Gura (antisense oligonucleotides that are synthesized are unmethylated, see p. 576). The prior art anticipates the claimed invention.

The rejection is maintained for claim 46. Applicant's arguments filed February 25, 2008 have been fully considered but they are not persuasive. Applicants have asserted that "claim 46 was re-written as an independent claim because Hutcherson et al did not administer any of SEQ ID NOs. 1-3 to humans in conjunction with a vaccine. Hutcherson et al does not provide a teaching that a CpG oligonucleotide is a component of the immunopotentiator being claimed. Thus, Hutcherson et al does not provide a teaching that an oligonucleotide having an unmethylated CpG dinucleotide be administered to a human in conjunction with a vaccine. Hutcherson et al does not inherently anticipate claim 46 because the method was not performed by Hutcherson et al.

However, it is noted that a US Patent is presumed valid and enabled. Since every patent is presumed valid (35 U.S.C. 282), and since that presumption includes the presumption of operability (Metropolitan Eng. Co. v. Coe, 78 F.2d 199, 25 USPQ 216 (D.C. Cir. 1935), examiners should not express any opinion on the operability of a patent. Affidavits or declarations attacking the operability of a patent cited as a reference must rebut the presumption of operability by a preponderance of the evidence. In re Sasse, 629 F.2d 675, 207 USPQ 107 (CCPA 1980).

Further, since in a patent it is presumed that a process if used by one skilled in the art will produce the product or result described therein, such presumption is not overcome by a mere showing that it is possible to operate within the disclosure

without obtaining the alleged product. In re Weber, 405 F.2d 1403, 160 USPQ 549 (CCPA 1969). It is to be presumed also that skilled workers would as a matter of course, if they do not immediately obtain desired results, make certain experiments and adaptations, within the skill of the competent worker. The failures of experimenters who have no interest in succeeding should not be accorded great weight. In re Michalek, 162 F.2d 229, 74 USPQ 107 (CCPA 1947); In re Reid, 179 F.2d 998, 84 USPQ 478 (CCPA 1950).

5. Claim 39 is objected to because of the following informalities: claim 39 depends from itself. Appropriate correction is required.

6. It is noted that the instant claims do not represent the elected species of SEQ ID NO: 1 and 6.

7. Newly submitted claims 37, 40-44, 47-53, 55 and 56 (as amended) are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the elected species (SEQ ID NO: 1, 6) are not representative of the claimed an immunostimulatory oligonucleotide that comprises a phosphate backbone modification, has greater than two unmethylated cytosine-guanine dinucleotides, wherein the oligonucleotide is at least eight nucleotides and includes a 5'TC dinucleotide.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 37, 40-44, 47-53,

55 and 56 (as amended) have been withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claim 45, 46 and 54 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 45 of copending Application No. 11/127797. Although the conflicting claims are not identical, they are not patentably distinct from each other because they both claim method of inducing (stimulating) the immune response of a subject to a vaccine comprising the vaccine and immunostimulatory oligonucleotide (unmethylated CpG, at least 8 nucleotides in length and has a phosphate backbone modification) and administering the composition.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record in related applications.

9. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the

advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to N. M. Minnifield whose telephone number is 571-272-0860. The examiner can normally be reached on M-F (8:00-5:30) Second Friday Off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-8975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/N. M. Minnifield/
Primary Examiner, Art Unit 1645
July 6, 2008